CLAIMS

What is claimed is:

1. A bioreactor comprising:
   a. a substrate having a first surface and an opposite second surface, defining a channel therein; and
   b. a plurality of chambers formed in the substrate, wherein each of the plurality of chambers is adapted for receiving cells in a liquid medium and formed with an open end, an opposite closed end and side walls, the open end and the closed end defining a depth, d, therebetween for the corresponding chamber, the sidewalls defining a width, w, therebetween for the corresponding chamber, and the chamber being in fluid communication with the channel through the open end.

2. The bioreactor of claim 1, wherein at least two of the plurality of chambers have depths or widths same or different from each other.

3. The bioreactor of claim 1, further comprising an inlet port in fluid communication with the channel, and an outlet port in fluid communication with the channel, wherein the inlet port and the outlet port are apart from each other along the channel.

4. The bioreactor of claim 1, wherein each of the plurality of chambers is adapted to receive and culture at least one predetermined type of cells.

5. The bioreactor of claim 4, wherein the cells are in the form of a biofilm.

6. The bioreactor of claim 4, wherein the cells comprise bacteria.

7. The bioreactor of claim 4, wherein the cells comprise protozoa.

8. The bioreactor of claim 4, further comprising a barrier for at least one of the chambers, wherein the barrier is positioned at the open end of the corresponding chamber and has a porosity to allow the corresponding chamber and the channel in fluid communication and allow at least one predetermined type of cells to permeate between the corresponding chamber

and the channel and at least another predetermined type of cells not to permeate between the corresponding chamber and the channel.

9. The bioreactor of claim 1, further comprising a biocompatible coating layer applied to the channel walls.

10. The bioreactor of claim 9, wherein the biocompatible coating layer comprises a material that may inhibit cell adhesion to the biocompatible coating layer.

11. The bioreactor of claim 1, further comprising a biocompatible coating layer applied to the sidewalls of each chamber.

12. The bioreactor of claim 11, wherein the biocompatible coating layer comprises a material that may inhibit cell adhesion to the biocompatible coating layer, enhance cell adhesion to the biocompatible coating layer, or function as a fluorescent marker or indicator of the state of cells.

13. The bioreactor of claim 1, further comprising at least one auxiliary port and an auxiliary channel in fluid communication with the auxiliary port and a corresponding one of the chambers for allowing individual control of the environment of the corresponding chamber.

14. The bioreactor of claim 13, wherein the individual control of the environment of the corresponding chamber includes delivery or removal of the cells, fluids or chemicals to the corresponding chamber or flushing the corresponding chamber.

15. The bioreactor of claim 13, further comprising at least one sample chamber and a plurality of sample channels in fluid communication with the sample chamber and a corresponding chamber, wherein the sample chamber is in fluid communication with at least one corresponding auxiliary channel that is in fluid communication with at least one corresponding auxiliary port, for allowing individual control of the environment of the corresponding sample chamber.

16. The bioreactor of claim 15, wherein the individual control of the environment of the corresponding sample chamber includes delivery or removal of the fluids or chemicals to the corresponding sample chamber.

17. The bioreactor of claim 15, wherein the sample chamber is adapted for receiving a sample of host material that provides exudates affecting the cells or biofilm in the corresponding chamber.

18. The bioreactor of claim 17, wherein the sample chamber is formed with a closed end and an opposite open end through which the host material can be received into or removed from the sample chamber.

19. The bioreactor of claim 18, further comprising a lid adapted for slidably covering or opening the open end of the sample chamber.

20. The bioreactor of claim 18, wherein the host material comprises soil.

21. The bioreactor of claim 1, further comprising at least one sample chamber in fluid communication with a corresponding chamber.

22. The bioreactor of claim 21, wherein the sample chamber is adapted for receiving a sample of host material that affects the cells or biofilm in the corresponding chamber.

23. The bioreactor of claim 22, wherein the sample chamber is formed with a closed end and an opposite open end through which the host material can be received into or removed from the sample chamber.

24. The bioreactor of claim 23, further comprising a lid adapted for slidably covering or opening the open end of the sample chamber.

25. The bioreactor of claim 1, wherein the substrate is fabricated from glass, Mylar, PDMS, silicon, a polymer, a semiconductor, or any combination of them.

26. The bioreactor of claim 1, further comprising means adapted for electrochemical measurements of the cells responsive to the liquid medium in at least one of the chambers.

27. The bioreactor of claim 26, wherein the means for electrochemical measurements comprises:

i.a counter electrode;

ii.a reference electrode; and

iii.a plurality of electrically conductive leads, where a first electrically conductive lead electrically couples the reference electrode to a corresponding edge connector pad, and a second electrically conductive lead electrically couples the counter electrode to a corresponding edge connector pad.

28. The bioreactor of claim 27, wherein the means for electrochemical measurements further comprises:

a plurality of individually addressable working electrodes and a plurality of corresponding amplifiers, each individually addressable working electrode being electrically coupled to a corresponding amplifier through a corresponding electrically conductive lead.

29. The bioreactor of claim 28, wherein the liquid medium comprises at least one analyte, and wherein the plurality of individually addressable working electrodes are adapted for capable of sensing the concentration of a single analyte of the liquid medium at multiple locations in a corresponding chamber or the concentrations of a plurality of analytes of the liquid medium at multiple locations in the corresponding chamber at a time period shorter than a characteristic reaction time related to at least one of cellular physiological activities of the cells.

30. The bioreactor of claim 29, wherein the plurality of individually addressable working electrodes are further adapted for capable of measuring the metabolic variables related to the cells responsive to the liquid medium at multiple locations in the corresponding chamber at a time period shorter than a characteristic reaction time related to at least one of cellular physiological activities of the cells.

31. The bioreactor of claim 28, further comprises a plurality of electrically conductive output leads, each electrically coupling a corresponding amplifier to an output device.

32. The bioreactor of claim 31, wherein the output device comprises a multiplexed potentiostat.

33. The bioreactor of claim 28, further comprising a plurality of controlling ports and a plurality of connection channels, wherein each of the connection channels is in fluid communication with a corresponding controlling port and the chamber.

34. The bioreactor of claim 33, further comprising a fluid control valve adapted for controlling the fluid communication between the plurality of controlling ports and the chamber.

35. The bioreactor of claim 34, wherein the fluid control valve comprises a pneumatic or mechanical valve.

36. The bioreactor of claim 35, further comprising a control port adapted for controlling the fluid control valve.

37. The bioreactor of claim 35, wherein the counter electrode and the reference electrode are positioned between the fluid control valve and the plurality of controlling ports.

38. The bioreactor of claim 37, wherein the liquid medium comprises at least one analyte, and wherein the plurality of individually addressable working electrodes are positioned between the fluid control valve and the plurality of controlling ports and adapted for capable of sensing the concentration of a single analyte of the liquid medium corresponding to multiple locations in a corresponding chamber, or the concentrations of a plurality of analytes of the liquid medium corresponding to multiple locations in the corresponding chamber, at a time period shorter than a characteristic reaction time related to at least one of cellular physiological activities of the cells.

39. The bioreactor of claim 38, wherein the plurality of individually addressable working electrodes are further adapted for capable of measuring the metabolic variables related to the cells responsive to the liquid medium at multiple locations corresponding to the corresponding chamber, at a time period shorter than a characteristic reaction time related to at least one of cellular physiological activities of the cells.

40. The bioreactor of claim 28, further comprises a plurality of electrically conductive output leads, each electrically coupling a corresponding amplifier to an output device.

41. The bioreactor of claim 40, wherein the output device comprises a multiplexed potentiostat.

42. The bioreactor of claim 27, wherein the reference electrode is adapted for electrochemical measurements of the cells responsive to the liquid medium in the plurality of chambers.

43. The bioreactor of claim 27, wherein in each of the plurality of chambers, a counter electrode is adapted for electrochemical measurements of the cells responsive to the liquid medium in a corresponding chamber to allow the plurality of chambers to be operated individually and the means for electrochemical measurements for the plurality of chambers to be activated for one or more chambers at a time sequentially.

44. The bioreactor of claim 1, further comprising means positioned in the channel and adapted for monitoring of the cells therein.

45. The bioreactor of claim 44, wherein the means for monitoring of the cells comprises at least one optical sensor and at least one lead in optical communication with a corresponding optical sensor.

46. The bioreactor of claim 45, wherein the optical sensor comprises at least one device selected from the group of an LED and photodiode pair, a fiber optic coupler, and an optical detecting head.

47. The bioreactor of claim 44, wherein the means for monitoring of the cells comprises at least one electrical sensor and at least one lead in electrical communication with a corresponding electrical sensor.

48. The bioreactor of claim 1, wherein the channel is adapted for allowing a bolus of selected chemicals to move along the channel.

49. A bioreactor comprising:

a. a substrate having a first surface and an opposite second surface; and

b. a plurality of array of chambers of chambers formed on the substrate, each being adapted for receiving cells in a liquid medium and comprising a channel and a plurality of chambers formed in the substrate, wherein each of the plurality of chambers is adapted for receiving cells in a liquid medium and formed with an open end, an opposite closed end and side walls, the open end and the closed end defining a depth, d, therebetween for the corresponding chamber, the sidewalls defining a width, w, therebetween for the corresponding chamber, and the chamber being in fluid communication with the channel through the open end, and wherein at least two of the plurality of chambers have depths same or different from each other.

50. The bioreactor of claim 49, wherein for at least one array of chambers of chambers at least two of the plurality of chambers have widths same or different from each other.

51. The bioreactor of claim 49, for at least one array of chambers of chambers, further comprising an inlet port in fluid communication with the channel, and an outlet port in fluid communication with the channel, wherein the inlet port and the outlet port are apart from each other along the channel.

52. The bioreactor of claim 49, wherein for at least one array of chambers each of the plurality of chambers is adapted to receive and culture at least one predetermined type of cells.

53. The bioreactor of claim 52, wherein the cells are in the forms of a plurality of biofilms.

54. The bioreactor of claim 53, wherein the cells comprise bacteria.

55. The bioreactor of claim 53, wherein the cells comprise protozoa.

56. The bioreactor of claim 53, for at least one array of chambers, further comprising a barrier for at least one of the chambers, wherein the barrier is positioned at the open end of the corresponding chamber and has a porosity to allow the corresponding chamber and the channel in fluid communication and allow at least one predetermined type of cells to permeate between the corresponding chamber and the channel and at least another predetermined

type of cells not to permeate between the corresponding chamber and the channel.

57. The bioreactor of claim 49, for at least one array of chambers, further comprising a biocompatible coating layer applied to the channel walls.

58. The bioreactor of claim 57, wherein the biocompatible coating layer comprises a material that may inhibit cell adhesion to the biocompatible coating layer.

59. The bioreactor of claim 49, for at least one array of chambers, further comprising a biocompatible coating layer applied to the sidewalls of each chamber.

60. The bioreactor of claim 59, wherein the biocompatible coating layer comprises a material that may inhibit cell adhesion to the biocompatible coating layer, enhance cell adhesion to the biocompatible coating layer, or function as a fluorescent marker or indicator of the state of cells.

61. The bioreactor of claim 49, for at least one array of chambers, further comprising at least one auxiliary port and an auxiliary channel in fluid communication with the auxiliary port and a corresponding one of the chambers for allowing individual control of the environment of the corresponding chamber.

62. The bioreactor of claim 61, wherein the individual control of the environment of the corresponding chamber includes delivery or removal of the cells, fluids or chemicals to the corresponding chamber or flushing the corresponding chamber.

63. The bioreactor of claim 49, wherein the substrate is fabricated from glass, Mylar, PDMS, silicon, a polymer, a semiconductor, or any combination of them.

64. The bioreactor of claim 49, for at least one array of chambers, further comprising means adapted for electrochemical measurements of the cells responsive to the liquid medium in at least one of the chambers.

65. The bioreactor of claim 64, wherein the means for electrochemical measurements comprises:

i.a counter electrode;

ii.a reference electrode; and

iii.a plurality of electrically conductive leads, where a first electrically conductive lead electrically couples the reference electrode to a corresponding edge connector pad, and a second electrically conductive lead electrically couples the counter electrode to a corresponding edge connector pad.

66. The bioreactor of claim 65, wherein the means for electrochemical measurements further comprises:

a plurality of individually addressable working electrodes and a plurality of corresponding amplifiers, each individually addressable working electrode being electrically coupled to a corresponding amplifier through a corresponding electrically conductive lead.

67. The bioreactor of claim 66, wherein the liquid medium comprises at least one analyte, and wherein the plurality of individually addressable working electrodes are adapted for capable of sensing the concentration of a single analyte of the liquid medium at multiple locations in a corresponding chamber or the concentrations of a plurality of analytes of the liquid medium at multiple locations in the corresponding chamber at a time period shorter than a characteristic reaction time related to at least one of cellular physiological activities of the cells.

68. The bioreactor of claim 67, wherein the plurality of individually addressable working electrodes are further adapted for capable of measuring the metabolic variables related to the cells responsive to the liquid medium at multiple locations in the corresponding chamber at a time period shorter than a characteristic reaction time related to at least one of cellular physiological activities of the cells.

69. The bioreactor of claim 66, further comprises a plurality of electrically conductive output leads, each electrically coupling a corresponding amplifier to an output device.

70. The bioreactor of claim 69, wherein the output device comprises a multiplexed potentiostat.

71. The bioreactor of claim 49, for at least one array of chambers, further comprising means positioned in the channel and adapted for monitoring of the cells therein.

72. The bioreactor of claim 71, wherein the means for monitoring of the cells comprises at least one optical sensor and at least one lead in optical communication with a corresponding optical sensor.

73. The bioreactor of claim 72, wherein the optical sensor comprises at least one device selected from the group of an LED and photodiode pair, a fiber optic coupler, and an optical detecting head.

74. The bioreactor of claim 71, wherein the means for monitoring of the cells comprises at least one electrical sensor and at least one lead in electrical communication with a corresponding electrical sensor.

75. The bioreactor of claim 72, wherein the channel is adapted for allowing a bolus of selected chemicals to move along the channel.

76. A method for culturing a plurality of biofilms, each containing a predetermined type of cells or cell growth conditions, comprising the steps of:

i. providing a bioreactor that has a substrate having a first surface and an opposite second surface and a plurality or array of chambers formed on the substrate, each being adapted for receiving cells in a liquid medium and comprising a channel and a plurality of chambers formed in the substrate, wherein each of the plurality of chambers is adapted for receiving cells in a liquid medium and formed with an open end, an opposite closed end and side walls, the open end and the closed end defining a depth, d, therebetween for the corresponding chamber, the sidewalls defining a width, w, therebetween for the corresponding chamber, and the chamber being in fluid communication with the channel through the open end, and wherein at least two of the plurality of chambers have depths different from each other; and

ii. culturing at least two biofilms in at least two arrays of chambers of the bioreactor.

77. The bioreactor of claim 76, further comprising the step of providing a bolus of selected chemicals to move along the channel for each of the at least two arrays of chambers.